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I-309/T cell activation gene-3 chemokine protects murine T cell lymphomas against dexamethasone-induced apoptosis.

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We have previously reported that cytokines such as IL-9, IL-4, and IL-6 protect murine thymic lymphoma cell lines against dexamethasone-induced apoptosis. A similar activity, which could not be ascribed to any of these factors, was found in a number of human T cell supernatants that enabled mouse BW5147 thymic lymphoma not only to escape apoptosis but also to maintain proliferation. The protein responsible for this activity was purified to homogeneity from the culture medium of activated leukemic T cells and was found to be identical with the I-309 chemokine. Half-maximal anti-apoptotic activity was obtained with approximately 1 ng/ml, a concentration considerably lower than that required for the monocyte chemotactic activity of this molecule, as measured on THP-1 cells. The purified I-309 also improved the survival of two other mouse thymic lymphoma cell lines. This activity was as potent as that of IL-9, which was the strongest anti-apoptotic factor found to date for these cells. Similar results were obtained for BW5147 cells with recombinant I-309 and with T cell activation gene-3, the murine homologue of I-309, but not with other members of the chemokine family, including IL-8, neutrophil-activating peptide-2, granulocyte chemotactic protein-2, macrophage inflammatory protein-1a, RANTES (regulated upon activation, normal T cell expressed and secreted), monocyte chemotactic protein-1 (MCP-1), and MCP-2. MCP-3, however, showed a minor, but significant effect in this model. Unlike that of IL-9, the activity of I-309 was completely inhibited in the presence of pertussis toxin, indicating the involvement of a G protein in this process.

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